

# Cyberknife radiosurgery for focal paravertebral recurrence after radical pleurectomy/decortication in malignant pleural mesothelioma

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## Abstract

We present a case of malignant pleural mesothelioma with focal relapse in the Azygos arch region after radical pleurectomy/decortication and adjuvant chemotherapy. Tumour recurrence was successfully treated by Cyberknife radiosurgery (70 Gy in five fractions). Patient remains disease-free at 40 months without any other treatment.

**Keywords:** Malignant pleural mesothelioma • Recurrence • Cyberknife

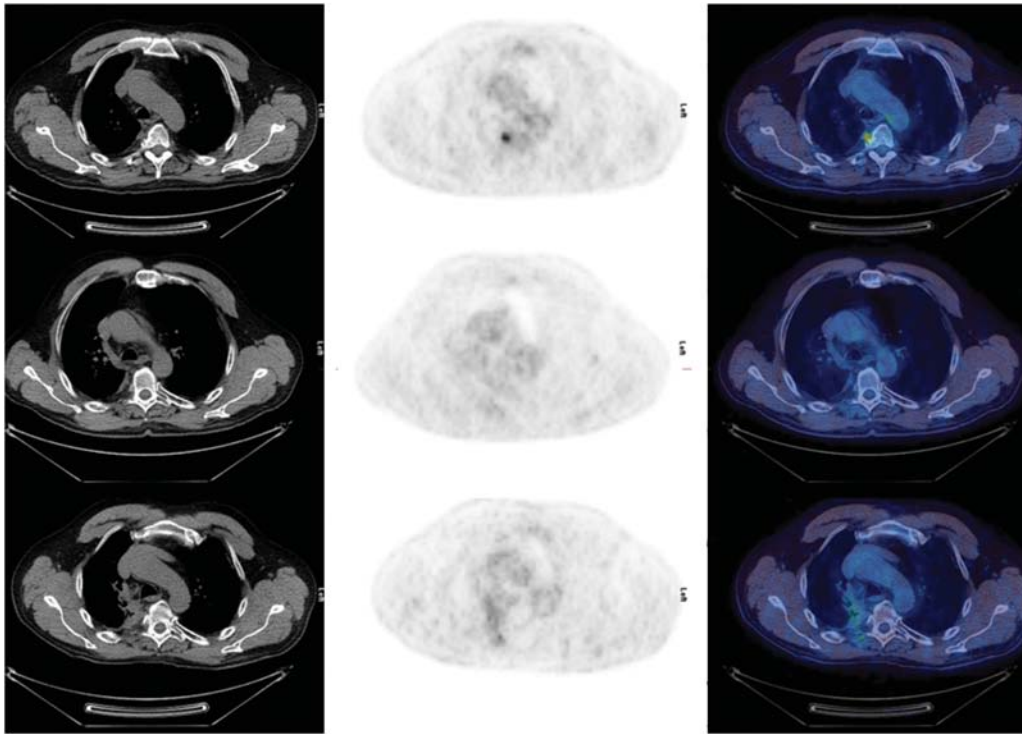
## CASE REPORT

A 62-year old male presented with pneumonia in July 2006. He had no significant medical history, was a life-long non-smoker, but disclosed asbestos exposure in the 1960's. Pleuritic pain persisted and he had a chest computed tomography (CT) in November 2006 which showed pleural plaques and right pleural thickening. In June 2007, repeat chest CT showed progression of right pleural thickening together with a 2.8 × 11 mm pleural nodule. Ultrasound-guided biopsy of the nodule showed a malignant pleural mesothelioma (MPM), of epithelioid subtype. Biology was within normal limits, haemoglobin 14.9 g/dl, WBC 4.6 × 10<sup>9</sup>, platelets 255 × 10<sup>9</sup> and fibrinogen 4.8 g/dl. Spirometry showed FEV1 3.45 (88%) and FVC 4.18 (84%). Considering the patient's excellent performance status, he was offered radical pleurectomy/decortication in August 2007, which confirmed an MPM, of epithelioid subtype stage IB. Pathology showed solid sheets of moderately pleomorphic epithelioid cells lying in a background of variably dense fibrosis. The tumour cells stained diffusely for calretinin and focally for CK5/6, but were negative for BerEP4 and CEA. The patient was discharged home at Day 6 and received prophylactic radiotherapy (21 Gy in three daily fractions) to his thoracotomy and drain sites within 6 weeks. He received six cycles of adjuvant chemotherapy with pemetrexed and cisplatin. Fluoro-deoxyglucose positron-emission tomography-computed tomography (PET-CT) performed in June 2008 showed three foci of abnormal uptake localized just above and below the level of the azygos arch, with a maximum standardized uptake value (SUVmax) of 7.3. Uptake was normal in the residual chest cavity and mediastinum (Fig. 1). Considering the localized nature of the relapse, the decision was made to offer radical radiotherapy with Cyberknife as a potentially curative option. Patient had two gold fiducial markers implanted under

CT guidance above and below the target volume and received 70 Gy in five daily fractions in July 2008. PET-CT performed 3 months after radiosurgery showed very low grade uptake in the Azygos arch region (SUVmax 1.3). PET-CT in July 2010 and January 2011 showed persistent low-grade uptake (SUVmax 3.3) in relation to the posterior aspect of the right upper lobe and Azygos arch region corresponding to features of localized radiation pneumonitis (Fig. 1). Clinically, the patient is only complaining of persistent right T4-T5 neuralgia. He remains active and disease-free 40 months after Cyberknife radiosurgery and >4 years after radical pleurectomy/decortication.

## DISCUSSION

MPM remains a major cause of death in patients exposed to asbestos [1]. At present, there is no known cure for MPM and median survival following diagnosis is often <12 months [2, 3]. Patients presenting with early stage disease and good performance status are suitable for multi-modality therapy involving surgery, radiotherapy and chemotherapy [4]. Extrapleural pneumonectomy, chemotherapy and adjuvant radiotherapy have been used at specialist centres in the past 25 years, but there is currently no evidence that this multi-modality regimen does improve survival or the quality of life [4, 5]. Recent publications have suggested that radical pleurectomy/decortication might be a better option in patients with early stage MPM [6]. We have been routinely offering radical pleurectomy/decortication instead of extrapleural pneumonectomy to patients with early stage MPM since 2007. Patients are routinely given prophylactic radiotherapy to the thoracotomy and drain sites at 4–6 weeks as well as adjuvant chemotherapy with pemetrexed and cisplatin (four to six cycles) to tackle residual microscopic disease.



**Figure 1:** PET-CT scans pre- and post-Cyberknife therapy. Axial slices are shown of the CT, PET and fused images of the PET-CT scans prior to Cyberknife treatment (top), 3 months after Cyberknife treatment (middle) and 3 years after Cyberknife treatment. The top image shows focal uptake in a pleural nodule (SUVmax 7.3) suspicious of disease recurrence. The middle image shows there is almost complete resolution of uptake 3 months after Cyberknife treatment (SUVmax 1.3). Increased uptake (SUVmax 3.3) 3 years after Cyberknife treatment is diffuse and in keeping with post-radiation changes (bottom image).

All our patients are followed up with PET-CT following multi-modality therapy [7]. We offer second-line chemotherapy or early phase trial drugs to patients diagnosed with relapse or disease progression.

In the present case, the patient was asymptomatic 6 months after completion of his multi-modality treatment and there was only one area of relapse on PET-CT. It seemed too aggressive to offer systemic treatment for such a localized disease. Radical radiotherapy is a recognized treatment modality in MPM, but previous reports have shown acute lung toxicity (radiation pneumonitis) and lack of clear benefit when it is administered following pleurectomy [8]. In the present case, the idea was to treat a limited volume in the paraspinal region without causing too much collateral damage to the lung, oesophagus or spinal cord. In addition, we had to work with a previously irradiated chest. Lastly, mesothelioma is a relatively radio-resistant tumour and we wanted to deliver a dose as high as possible to the target volume. Altogether, Cyberknife radiosurgery appeared to be an excellent option, based on recent experience in patients with a previously irradiated spine or in patients with paravertebral tumours with doses of 70 Gy in five fractions [9].

Regular follow-up showed progressive decrease in the target area SUVmax, confirming the efficacy of treatment. Persistent intercostal neuralgia could represent a side effect of stereotactic radiotherapy, as the origin of the pain seems to be precisely the irradiated paravertebral region.

Although Cyberknife radiosurgery is unlikely to represent an adequate treatment modality in most patients with MPM, it may represent an attractive curative or palliative treatment option in some patients with very limited and localized disease [10].

**Conflict of interest:** none declared.

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